Citation:

Chen SC, Judd JT, Kramer M, Meijer GW, Clevidence BA, Baer DJ. Phytosterol intake and dietary fat reduction are independent and additive in their ability to reduce plasma LDL cholesterol. *Lipids.* 2009 Mar; 44 (3): 273-281. Epub 2009 Jan 15.

PubMed ID: 19145455

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effects of plant sterols (PS) in the context of two background diets (American diet and Step I diet) differing in fat level and composition on blood lipids and lipoprotein levels.

Inclusion Criteria:

- Mildly hypercholesterolemic men
- Postmenopausal women.

Exclusion Criteria:

Postmenopausal women receiving hormone replacement therapy (HRT).

Description of Study Protocol:

Recruitment

Not available.

Design

Randomized, double-blind, cross-over trial for four experimental diets and 23 days for each.

Dietary Intake/Dietary Assessment Methodology

All foods are provided by the Beltsville Human Nutrition Research Center at USDA.

Blinding Used

Yes.

Intervention

Each of the following experimental diet was lasted for 23 days and there was not washout between periods:

- Typical American Diet (TAD) and No PS: THE TAD was designed to contain 34% of energy from fat with a ratio of saturated fatty acids to total monounsaturated fatty acids to total polyunsaturated fatty acids of 1:1:0.5+ 0 PS
- Step 1 and No PS: The step 1 diet was designed to contain less than 30% of energy from fat and less than 7.0% from saturated fat with a ratio of saturated to total monounsaturated to total polyunsaturated fatty acids of 1:1.5:1+ 0 PS
- Typical American Diet (TAD) and PS: TAD + 3.3g per day PS (1.8g per serving of PS as ester from vegetable oil sources)
- Step 1 and No PS: Step 1 diet + 3.3g per day PS (1.8g per serving of PS as ester from vegetable oil sources).

Statistical Analysis

- Mixed-effects model for analysis of the data for repeated measurements
- The T-test was used to compare the mean baseline values of men and women.

Data Collection Summary:

Timing of Measurements

Baseline (two samples) and the end of 22 days (day 22 and 24).

Dependent Variables

- TC, HDL-cholesterol and TAG: Measured enzymatically with commercial kits (Sigma Chemical Company)
- LDL: Calculated using the Friedewald equation
- Apoliproteins A1 (Apo A1) and B (Apo B): measured by rate nephelometry (Beckman ICS Immunochemical Analyzer).

Independent Variables

Four experimental diet groups:

- Two levels of PS (zero and 3.3g per day)
- Two background diets with different fat content
    - Typical American Diet (TAD (total fat=33.5%; saturated fat=13.2% of energy)
    - Step 1 Diet (total fat=26.4%; saturated fat=7.7% of energy).

Control Variables

Relative amounts of all nutrients, other than those providing different amounts and types of fat, were constant for all subjects.

Description of Actual Data Sample:

- *Initial N:* 23 (14 men, 9 women)

- *Attrition (final N):* 22
- *Age:* Mean=51.7; SD=2.4
- *Ethnicity:* Not available
- *Other relevant demographics:* Not available
- *Anthropometrics:* BMI: 28.0±0.6kg/m^2
- *Location:* US.

Summary of Results:

Table 1: Effect of Diet and PS on Plasma Lipids and Lipoproteins

Variables	Treatment 1				Diet Effect		PS Effect		P-value (F Test)		
	Step 1		TAD								
	-PS	+PS	-PS	+PS	Step 1	TAD	-PS	+PS	Diet	PS	Diet * PS
TAG (mmol/L)	1.532	1.41	1.52	1.41	1.47	1.46	1.52	1.41	0.87	0.005	0.69
TC (mmol/L)	5.31^{c}	4.83^{a}	5.55^{d}	5.06^{b}	5.07	5.30	5.43	4.94	<0.0001	<0.0001	0.91
HDL-C (mmol/L)	1.24^{a}	1.25^{a}	1.31^{b}	1.32^{b}	1.25	1.33	1.29	1.29	<0.0001	0.28	0.52
LD-C (mmol/L)	3.38^{b}	2.95^{a}	3.55^{b}	3.10^{a}	3.17	3.22	3.46	3.03	0.002	<0.0001	0.79
TC/HDL-C	4.53^{b}	4.12^{a}	4.47^{b}	4.03^{a}	4.33	4.25	4.50	4.07	0.1062	<0.0001	0.75
Apo A1 (g/L)	1.40^{a}	1.40^{a}	1.44^{ab}	1.45^{b}	1.40	1.44	1.42	1.42	0.0006	0.73	0.75
ApoB (g/L)	0.80^{b}	0.77^{a}	0.85^{c}	0.77^{a}	0.79	0.81	0.82	0.77	0.007	<0.0001	0.0004
Apo B/Apo A1	0.59^{b}	0.56^{a}	0.61^{b}	0.54^{a}	0.58	0.58	0.60	0.55	0.98	<0.0001	0.001

[1] Among four treatments, values in a row with different superscripts differ, P<0.05

[2] LS mean

[3] In the presence of PS, no diet effect was detected for plasma Apo B level (P=0.9982). In the absence of PS, Apo B after TAD feeding was higher than that after Step 1 feeding (P=0.0006)

[4] The PS induced lowering of Apo B/Apo A1 was greater after TAD feeding (11.5% reduction, P=0.0001) than after Step 1 feeding (5.1% reduction, P=0.0227)

Author Conclusion:

The findings of the present study indicate that the total cholesterol and LDL cholesterol lowering

effects resulting from PS are independent of, and additive to, the effect of dietary fat reduction when changing from the typical American diet to the Step 1 diet.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	N/A
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes

3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A

6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes

8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	No
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	No